

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

It is agreed that a new Figure 7 will be submitted labeled "Prior Art".

Paragraph 1 of the Specification has been amended as follows: --

[0001] This application -- is a 371 of PCT/US03/25230, filed 08/13/2003 and -- claims the benefit of U.S. Provisional Patent Application Serial No. 60/403,575, filed August 14, 2002, and U.S. Provisional Patent Application Serial No. 60/471,603, filed May 19, 2003. -- .

The Claims have been amended as follows:

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Currently Amended) A method for crossflow membrane filtration of a poly-disperse suspension, said method comprising:

selecting a poly-disperse suspension having a distribution of particle sizes;
determining particle size distribution of the poly-disperse suspension;
determining equivalent spherical radii of the particles;
determining viscosity of the suspension;
determining maximum back-transport velocity (u_i) for all particles;
estimating maximum aggregate packing volume fraction (ϕ_{st}) for all particles at a wall of the filtration membrane from geometric considerations;
selecting the particle that gives a minimum permeation flux at a given filtration membrane shear rate, wherein the selected particle has a radius (a_i);

determining a predicted permeation flux (J);
determining packing density ϕ_{wi} at a membrane wall for each particle size (a_j for $j \neq i$) at the predicted permeation flux;
determining interstitial packing density ($\phi_{w\text{interstice}}$) of particles in the suspension which are the smallest;
determining minimum pore diameter ($2r_{\text{minimum}}$) based on the packing density of each particle;
estimating yield of a target species in the filtration permeate by calculating observed sieving coefficient (S_o) for the target species, thereby predicting pressure independent permeation flux and target molecule yield in a permeate resulting from crossflow membrane filtration of particles in the poly-disperse suspension during crossflow filtration;
optimizing conditions for filtration based on the prediction of pressure independent permeation flux and target molecule yield to design a filtration system for the said poly-disperse suspension; and
filtering the selected poly-disperse suspension using the designed filtration system.

2. (Original) The method according to claim 1, wherein said determining viscosity of the suspension is carried out by using a modified Einstein-Smoluchowski equation: $\eta/\eta_0 = 1 + 2.5\phi_b + k_1\phi_b^2$, where η is bulk fluid viscosity (kg/m.s) of the suspension, η_0 is bulk fluid viscosity of the suspension without solute (kg/m.s), k_1 is particle shape factor (-), and ϕ_b is particle volume fraction in the bulk suspension (-).

3. (Original) The method according to claim 1, wherein said determining viscosity of the suspension is carried out by experiment.

4. (Currently Amended) The method according to claim 1, wherein said determining maximum back-transport velocity (u_i) comprises:

calculating Brownian diffusion (J_B) for all particles, where
$$J_B = 0.114(\gamma\kappa^2 T^2 / \eta^2 a^2 L)^{1/3} \ln(\phi_w/\phi_b);$$

calculating inertial lift (J_l) for all particles, where $J_l = 0.036\rho a^3 \gamma^2 / \eta$;
calculating shear induced diffusion (J_s) for all particles where $J_s = 0.078(a^4/L)^{1/3} \gamma \ln(\phi_w/\phi_b)$, wherein γ is wall shear rate (s^{-1}), κ is Boltzmann constant ($J/mol K$), T is temperature (K), η is bulk fluid viscosity ($kg/m.s$), a_i is radius of species i (m), L is tube length (m), ϕ_w is particle volume fraction at the filtration membrane (-), ϕ_b is the particle volume fraction in the bulk suspension (-), and ρ is particle density (kg/m^3); and
selecting J_{max} for each particle size, wherein $J_{max} = u_i$, whereby maximum back-transport for each particle size is determined.

5. (Original) The method according to claim 1, wherein said estimating maximum aggregate packing volume fraction (ϕ_M) at the membrane wall for a suspension comprises:

determining particle size (a_i) of species (i) in the suspension;
determining if the size ratio of the particles is > 10 , such that $a_{i+1} > 10a_i$ for all a_i ;
and

calculating the maximum aggregate packing volume fraction (ϕ_{Mn}) by $\phi_{Mn} = \phi_m + \phi_m(1 - \phi_{Mn-1})$, where $\phi_M = \phi_m$ is set to 0.64 when the size ratio of the particles is > 10 , such that $a_{i+1} > 10a_i$ for all a_i .

6. (Original) The method according to claim 5, wherein the suspension comprises 3 particle sizes and wherein $a_1 > 10a_2 > 100a_3$, said method further comprising:

calculating $\phi_M = \phi_m + \phi_m(1 - \phi_m) + 0.74[1 - \{\phi_m + \phi_m(1 - \phi_m)\}]$,
wherein ϕ_m is set to 0.64.

7. (Currently Amended) The method according to claim 1, wherein said estimating maximum aggregate packing volume fraction (ϕ_M) at the membrane wall for a suspension comprising two particles sizes, such that $a_1 > 10a_2$, is carried out by calculating $\phi_M = \phi_m + 0.74(1 - \phi_m)$, where ϕ_m is set to 0.64.

8. (Original) The method according to claim 1, wherein said estimating maximum aggregate packing volume fraction (ϕ_M) at the membrane wall comprises:

- calculating a maximum radius ratio of all particles;
- determining if said maximum radius ratio is < 10 ; and
- setting ϕ_M as 0.68, where said maximum radius ratio is < 10 .

9. (Currently Amended) The method according to claim 1, wherein said selecting the particle that gives the minimum permeation flux (J) comprises:

- calculating Brownian diffusion (J_B) for all particles, where $J_B = 0.114(\gamma\kappa^2 T^2/\eta^2 a^2 L)^{1/3} \ln(\phi_w/\phi_b)$;
- calculating inertial lift (J_l) for all particles, where $J_l = 0.036\rho a^3 \gamma^2/\eta$;
- calculating shear induced diffusion (J_s) for all particles, where $J_s = 0.078(a^4/L)^{1/3} \gamma \ln(\phi_w/\phi_b)$, wherein γ is wall shear rate (s^{-1}), κ is Boltzmann constant (J/mol K), T is temperature (K), η is bulk fluid viscosity (kg/m.s), a_i is radius of species i (m), L is tube length (m), ϕ_w is particle volume fraction at the membrane wall (-), ϕ_b is the particle volume fraction in the bulk suspension (-), and ρ is particle density (kg/m³);
- determining a J_{max} value for each particle size; and
- selecting a J_{max} value from among all J_{max} values that is the lowest, thereby selecting the minimum permeation flux (J).

10. (Currently Amended) The method according to claim 1, wherein said determining packing density at the membrane wall (ϕ_{wj}) for all particles at the predicted permeation flux (a_j for $j \neq i$) comprises:

back-calculating the value of ϕ_{wj} such that ϕ_{wj} gives the predicted permeation flux (J) of selected particle size (a_i) using the equation for back-transport that establishes maximum back transport for each particle size (a_j for $j=i$), wherein the equation is either $J_B = 0.114(\gamma\kappa^2 T^2/\eta^2 a^2 L)^{1/3} \ln(\phi_w/\phi_b)$ or $J_s = 0.078(a^4/L)^{1/3} \gamma \ln(\phi_w/\phi_b)$, or $J_l = 0.036\rho a^3 \gamma^2/\eta$, where γ is wall shear rate (s^{-1}), κ is Boltzmann constant (J/mol K), T is temperature (K), η is bulk fluid viscosity (kg/m.s), a_i is radius of species i (m), L is tube length (m), ϕ_w is particle volume fraction

at the membrane wall (-), ϕ_b is the particle volume fraction in the bulk suspension (-), and ρ is particle density (kg/m³).

11. (Original) The method according to claim 10, wherein said determining packing density further comprises:

determining if the predicted permeation flux is established by inertial lift (J_l) for one particle type;

determining if $u_{jl} \geq 10J$; and

setting $\phi_{wj} = 0$, when one particle type is established by inertial lift (J_l) and $u_{jl} \geq 10J$.

12. (Original) The method according to claim 10, wherein said determining packing density further comprises:

determining if the predicted permeation flux is established by inertial lift (J_l) for one particle type;

determining if $u_{jl} < 10J$; and

determining packing density (ϕ_{wj}) by $\phi_{wjl} = \phi_M - \sum \phi_{wj}$ when $u_{jl} < 10J$ and one particle type is established by inertial lift.

13. (Original) The method according to claim 10, wherein said determining packing density further comprises:

determining if permeation flux is established by inertial lift (J_l) for more than one particle type;

determining if $u_{jl} < 10J$ for the particles; and

determining packing density by $\phi_{wj} = \phi_M - \sum \phi_{wj}$ when $u_{jl} < 10J$ and permeation flux is established by inertial lift for more than one particle type.

14. (Original) The method according to claim 10, wherein said determining packing density further comprises:

determining if permeation flux is established by J_l for more than one particle type ($j11, j12, \dots, j1n$); and

determining packing density at the membrane wall by

$\phi_{wj11} + \phi_{wj12} = \phi_M - \sum \phi_{wj},$ wherein $\phi_{wj11} : \phi_{wj12} = \phi_{bj11} u_{j12} : \phi_{bj12} u_{j11}$, where $j \neq j11$ or $j12$ and $u_{j11}, u_{j12} < 10J$, when permeation flux is established by J_1 for more than one particle type.

15. (Original) The method according to claim 1, wherein said determining interstitial packing density ($\phi_{wiinterstice}$) of the smallest particle is carried out by

$\phi_{wiinterstice} = \phi_{wicorrected} / (1 - \sum \phi_{wjcorrected}),$ wherein $\phi_{wicorrected} = \phi_M [(\phi_{wi}) / \sum \phi_{wi}],$ where ϕ_{wi} is the particle volume fraction at the membrane wall (-) for particle i .

16. (Original) The method according to claim 1, wherein said determining minimum pore diameter ($2r_{\text{minimum}}$) is carried out using

$2r_{\text{minimum}} = a_i \{ \sqrt{2} [4(4/3)\pi / \phi_{wiinterstice}]^{1/3} - 2 \},$ where a is radius of species i (m) and r_{minimum} is a minimum equivalent cake void radius for all cake types (m).

17. (Original) The method according to claim 1, wherein said estimating yield of a target species comprises:

calculating observed sieving coefficient (S_o), where $S_o = S_o / ((1 - S_a) \exp(-J/k) + S_a),$ wherein actual sieving coefficient S_a is obtained from

$S_a = (S_x \exp(Pe_m)) / (S_x + \exp(Pe_m) - 1),$ wall Peclet number, Pe_m is obtained from $Pe_m = (J \delta_m / D)(S_x / \varepsilon \phi K_d),$ where J is permeation flux (m/s), δ_m is taken as the side of the face centered cube of the particles of radius a_i that forms the controlling cake for transmission, $\delta_m = a = a_i [(4(4/3)\pi / \phi_{wiinterstice})]^{1/3},$ D is molecular diffusion coefficient (m^2/s), intrinsic sieving coefficient S_x is obtained from $S_x = (1 - \lambda)^2 [2 - (1 - \lambda)^2] \exp(-0.7146\lambda^2),$ $\lambda = r_s / r_{\text{min}},$ where r_s is solute radius (m) and r_{min} is a minimum equivalent cake void radius for all cake types (m), ϕ is equilibrium partition coefficient between membrane pore and suspension (-), ε is cake/membrane porosity (-), K_d is hindrance factor for diffusive transport (-), and k is mass transfer coefficient (m/s).

18. (Original) The method according to claim 1, wherein crossflow-filtration is carried out in a diafiltration mode, and the yield of the target species is estimated after N_d

diavolumes as Yield = $1 - \exp(-N_d S_{\text{average}})$ where S_{average} is average observed sieving coefficient during diafiltration (-), where $S_o = S_o / ((1 - S_o) \exp(-J/k) + S_o)$, where actual sieving coefficient S_o is obtained from $S_o = (S_o \exp(Pe_m)) / (S_o + \exp(Pe_m) - 1)$, where J is permeation flux (m/s), wall Peclét number, Pe_m , is obtained from $Pe_m = (J \delta_m / D) (S_x / \varepsilon \phi K_d)$, where δ_m is taken as the side of the face centered cube of the particles of radius a_i that forms the controlling cake for transmission, where $\delta_m = a = a_i [(4(4/3)\pi) / \phi_{\text{interstice}}]^{1/3}$, D is molecular diffusion coefficient (m^2/s), intrinsic sieving coefficient S_x is obtained from $S_x = (1 - \lambda)^2 [2 - (1 - \lambda)^2] \exp(-0.7146\lambda^2)$, $\lambda = r_s / r_{\min}$, where r_s is solute radius (m) and r_{\min} is a minimum equivalent cake void radius for all cake types (m), ϕ is equilibrium partition coefficient between membrane pore and suspension (-), ε is cake/membrane porosity (-), K_d is hindrance factor for diffusive transport (-), and k is mass transfer coefficient (m/s).

19. (Original) The method according to claim 1 further comprising: re-calculating packing density for all particle sizes if packing constraints are not satisfied based on initial determination of packing densities of the particles at the wall.

20. (Currently Amended) The method according to claim 19 further comprising:

correcting packing density using $\phi_{\text{wicorrected}} = \phi_M [(\phi_{\text{w}i}) / \sum \phi_{\text{w}i}]$;
reevaluating J for the particle size selected as having the minimum permeation flux based on $\phi_{\text{wicorrected}} = \phi_M [(\phi_{\text{w}i}) / \sum \phi_{\text{w}i}]$; and
reevaluating maximum back-transport velocity (u_i).

21. (Original) The method according to claim 20 further comprising: repeating the steps of claim 17 until a desired packing constraint is met.

22. (Original) The method according to claim 1 further comprising: refining the yield of the target species.

23. (Original) The method according to claim 22, wherein said refining the yield comprises:

determining whether the suspension has a low, intermediate, or high operating shear rate leading to different yield regimes, wherein a suspension at a low operating shear rate leads to an $S_o \geq 0.75$ corresponding to a yield ≥ 0.95 , an intermediate operating shear rate leads to $0 < S_o < 0.75$ corresponding to yield from 0 to 95%, or a high operating shear rate leads to an $S_o \approx 0$, wherein $S_o = S_a / ((1 - S_a) \exp(-J/k) + S_a)$, wherein actual sieving coefficient S_a is obtained from $S_a = (S_x \exp(Pe_m)) / (S_x + \exp(Pe_m) - 1)$, wall Pecllet number, Pe_m is obtained from $Pe_m = (J \delta_m / D) (S_x / \varepsilon \phi K_d)$, where J is permeation flux (m/s), δ_m is taken as the side of the face centered cube of the particles of radius a_i that forms the controlling cake for transmission, $\delta_m = a = a_i$ $[(4(4/3)\pi) / \phi_{interstice}]^{1/3}$, D is molecular diffusion coefficient (m²/s), intrinsic sieving coefficient S_x is obtained from $S_x = (1 - \lambda)^2 [2 - (1 - \lambda)^2] \exp(-0.7146\lambda^2)$, $\lambda = r_s / r_{min}$, where r_s is solute radius (m) and r_{min} is a minimum equivalent cake void radius for all cake types (m), ϕ is equilibrium partition coefficient between membrane pore and suspension (-), ε is cake/membrane porosity (-), K_d is hindrance factor for diffusive transport (-), and k is mass transfer coefficient (m/s).

24. (Original) The method according to claim 23, wherein an intermediate operating shear rate is determined as leading to $0 < S_o < 0.75$, said method further comprising:
calculating stagnant film flux (J) equation for non-retentive membranes wherein $J = k \ln [(\phi_{wi} - \phi_{permeate}) / (\phi_{bi} - \phi_{permeate})] \cong k \ln [\phi_{wi} / \phi_{bi} (1 - S_o)]$, wherein $(\phi_{wi} \gg \phi_{permeate})$; and
correcting S_o by replacing $J =$ solvent permeation flux (m/s) with the stagnant film flux (J) equation for non-retentive membranes in the equation for observing sieving coefficient, S_o , where $S_o = S_a / ((1 - S_a) \exp(-J/k) + S_a)$.

25. (Original) The method according to claim 1 further comprising:
constructing a plot of the predicted permeation flux and yield versus wall shear rate, thereby predicting permeation flux and target molecule yield of the poly-disperse suspension during microfiltration.

26. (Original) The method according to claim 1, wherein filtration is selected from the group consisting of microfiltration and ultrafiltration.

27. (Original) The method according to claim 1, wherein filtration is carried out with a filter selected from the group consisting of a flat sheet filter, hollow-fiber filter, and a helical filter.

28. (Original) The method according to claim 1, wherein the suspension is selected from the group consisting of streams from biomedical and bio-processing industries, waste water, surface water, environmental pollutants, industrial waste streams, and industrial feed streams.

29. (Original) The method according to claim 28, wherein the suspension is a stream from biomedical and bio-processing industries selected from the group consisting of proteins, cells, nucleic acids, colloids, milk, and suspended particles.

30. (Currently Amended) A method for crossflow membrane filtration of a poly-disperse suspension, said method comprising:

selecting a poly-disperse suspension having a distribution of particle sizes;

providing a predicted permeation flux (J);

determining packing density for all particle sizes at the predicted permeation flux;

determining interstitial packing density ($\phi_{w\text{interstice}}$) of particles in the suspension which are smallest, thereby determining packing density at the membrane wall of particles of the poly-disperse suspension;

optimizing conditions for filtration based on the said packing density to design a filtration system for the said poly-disperse suspension; and

filtering the selected poly-disperse suspension using the designed filtration system.

31. (Currently Amended) The method according to claim 30, wherein said determining packing density at the membrane wall (ϕ_{wj}) for all other particles at the predicted permeation flux (a_j for $j \neq i$) comprises:

back-calculating the value of ϕ_{wj} such that ϕ_{wj} gives the predicted permeation flux (J) of selected particle size (a_i), using the equation for back-transport that establishes maximum

back transport for each particle size (a_j for $j=i$), wherein the equation is either $J_B = 0.114(\gamma\kappa^2 T^2/\eta^2 a^2 L)^{1/3} \ln(\phi_w/\phi_b)$ or $J_S = 0.078(a^4/L)^{1/3} \ln(\phi_w/\phi_b)$, or $J_I = 0.036\rho a^3 \gamma^2/\eta$, where γ is wall shear rate (s^{-1}), κ is Boltzmann constant ($J/mol K$), T is temperature (K), η is bulk fluid viscosity (kg/m.s), a_i is radius of species i (m), L is tube length (m), ϕ_w is particle volume fraction at the membrane wall (-), ϕ_b is the particle volume fraction in the bulk suspension (-), and ρ is particle density (kg/m³).

32. (Original) The method according to claim 31, wherein said determining packing density further comprises:

determining if the predicted permeation flux is established by inertial lift (J_I) for one particle type;

determining if $u_{jl} \geq 10J$; and

setting $\phi_{wj} = 0$, when one particle type is established by inertial lift (J_I).

33. (Original) The method according to claim 31, wherein said determining packing density further comprises:

determining if the predicted permeation flux is established by inertial lift (J_I) for one particle type;

determining if $u_{jl} < 10J$; and

determining packing density (ϕ_{wj}) by $\phi_{wj} = \phi_M - \sum \phi_w$ when $u_{jl} < 10J$ and one particle type is established by inertial lift.

34. (Original) The method according to claim 31, wherein said determining packing density further comprises:

determining if permeation flux is established by inertial lift (J_I) for more than one particle type;

determining if $u_{jl} < 10J$ for the particles; and

determining packing density by $\phi_{wj} = \phi_M - \sum \phi_w$ when $u_{jl} < 10J$ and permeation flux is established by inertial lift for more than one particle type.

35. (Original) The method according to claim 31, wherein said determining packing density further comprises:

determining if permeation flux is established by J_1 for more than one particle type (j11, j12, . . . j1n); and

determining packing density at the membrane wall by

$\phi_{wj11} + \phi_{wj12} = \phi_M - \sum \phi_{wj}$, wherein $\phi_{wj11} : \phi_{wj12} = \phi_{wj11} u_{j12} : \phi_{wj12} u_{j11}$, where $j \neq j11$ or j12 and $u_{j11}, u_{j12} < 10J$, when permeation flux is established by J_1 for more than one particle type.

36. (Original) The method according to claim 30, wherein said determining interstitial packing density ($\phi_{wiinterstice}$) of the smallest particle is carried out by $\phi_{wiinterstice} = \phi_{wicorrected} / (1 - \sum \phi_{wicorrected})$, wherein $\phi_{wicorrected} = \phi_M [(\phi_{wi}) / \sum \phi_{wi}]$, where ϕ_{wi} is the particle volume fraction at the membrane wall (-) for particle i .

37. (Original) The method according to claim 31 further comprising:

re-calculating packing density for all particle sizes and

determining if packing constraints are not satisfied based on initial determination of packing densities of the particles at the wall.

38. (Currently Amended) The method according to claim 37 further comprising:

correcting packing density by using $\phi_{wicorrected} = \phi_M [(\phi_{wi}) / \sum \phi_{wi}]$;

reevaluating J for the particle size selected as having the minimum permeation flux based on $\phi_{wicorrected} = \phi_M [(\phi_{wi}) / \sum \phi_{wi}]$; and

reevaluating maximum back-transport velocity (u_i).

39. (Original) The method according to claim 30, wherein filtration is selected from the group consisting of microfiltration and ultrafiltration.

40. (Currently Amended) A method for crossflow membrane filtration of a poly-disperse suspension, said method comprising:

selecting a poly-disperse suspension having a distribution of particle sizes;

determining viscosity of the suspension;
determining maximum back-transport velocity (u_i) for all particles;
estimating maximum aggregate packing volume fraction (ϕ_M) for all particles at a wall of the filtration membrane from geometric considerations;
selecting the particle that gives a minimum permeation flux at a given filtration membrane shear rate, wherein the selected particle has a radius (a_i);
determining a predicted permeation flux (J);
determining packing density (ϕ_{wj}) at the membrane wall for each particle size (a_j for $j \neq i$) at the predicted permeation flux, thereby predicting pressure independent permeation flux for crossflow membrane filtration of the poly-disperse suspension;
optimizing conditions for filtration based on the prediction of permeation flux to design a filtration system for the selected poly-disperse suspension; and
filtering the selected poly-disperse suspension using the designed filtration system.

41. (Original) The method according to claim 40 further comprising:
re-calculating packing density for all particle sizes if packing constraints are not satisfied based on initial determination of packing densities at the wall.

42. (Currently Amended) The method according to claim 41 further comprising:

correcting packing density using $\phi_{wicorrected} = \phi_M [(\phi_{wi})/\sum \phi_{wj}]$;
reevaluating J for the particle size selected as having the minimum permeation flux based on $\phi_{wicorrected} = \phi_M [(\phi_{wi})/\sum \phi_{wj}]$; and
reevaluating maximum back-transport velocity (u_i).

43. (Original) The method according to claim 40, wherein said determining viscosity of the suspension is carried out by using a modified Einstein-Smoluchowski equation:
 $\eta/\eta_0 = 1 + 2.5\phi_b + k_1\phi_b^2$, where η is bulk fluid viscosity (kg/m.s) of the suspension, η_0 is bulk

fluid viscosity of the suspension without solute (kg/m.s), k_1 is particle shape factor (-), and ϕ_b is particle volume fraction in the bulk suspension.

44. (Original) The method according to claim 40, wherein said determining viscosity of the suspension is carried out by experiment.

45. (Currently Amended) The method according to claim 40, wherein said determining maximum back-transport velocity (u_i) comprises:

calculating Brownian diffusion (J_B) for all particles, where

$$J_B = 0.114(\gamma\kappa^2 T^2/\eta^2 a^2 L)^{1/3} \ln(\phi_w/\phi_b);$$

calculating inertial lift (J_l) for all particles, where $J_l = 0.036\rho a^3 \gamma^2/\eta$;

calculating shear induced diffusion (J_s) for all particles, where $J_s = 0.078(a^4/L)^{1/3} \gamma \ln(\phi_w/\phi_b)$, and wherein γ is wall shear rate (s^{-1}), κ is Boltzmann constant ($J/mol K$), T is temperature (K), η is bulk fluid viscosity (kg/m.s), a_i is radius of species i (m), L is tube length (m), ϕ_w is particle volume fraction at the membrane wall (-), ϕ_b is the particle volume fraction in the bulk suspension (-), and ρ is particle density (kg/m^3); and

selecting J_{max} for each particle size, wherein $J_{max} = u_i$, thereby determining maximum back-transport for each particle.

46. (Original) The method according to claim 40, wherein said estimating maximum aggregate packing volume fraction(ϕ_M) at the membrane wall for a suspension comprises:

determining particle size (a_i) of species (i) in the suspension;

determining if the size ratio of the particles is > 10 , such that $a_{i+1} > 10a_i$ for all a_i ; and

calculating the maximum aggregate packing volume fraction(ϕ_{Mn}) by

$\phi_{Mn} = \phi_m + \phi_m (1 - \phi_{Mn-1})$, where $\phi_M = \phi_m$ set to 0.64, when the size ratio the particles is > 10 , such that $a_{i+1} > 10a_i$ for all a_i .

47. (Original) The method according to claim 40, wherein the suspension comprises 3 particle sizes and wherein $a_1 > 10a_2 > 100a_3$, said method further comprising:

calculating $\phi_M = \phi_m + \phi_m (1 - \phi_m) + 0.74[1 - \{\phi_m + \phi_m (1 - \phi_m)\}]$,

wherein ϕ_m is the maximum packing volume fraction for monodisperse spheres set to 0.64.

48. (Original) The method according to claim 40, wherein said estimating maximum aggregate packing volume fraction (ϕ_M) at the membrane wall comprises:

calculating a maximum radius ratio of all particles;

determining if said maximum radius ratio is < 10 ; and

setting ϕ_M as 0.68, where said maximum radius ratio is < 10 .

49. (Original) The method according to claim 40, wherein said estimating maximum aggregate packing volume fraction (ϕ_M) at the membrane wall for a suspension comprising two particles, such that $a_1 > 10 a_2$, is carried out by calculating $\phi_M = \phi_m + 0.74 (1 - \phi_m)$, where ϕ_m is set to 0.64.

50. (Currently Amended) The method according to claim 40, wherein said selecting the particle that gives a minimum permeation flux (J) comprises:

calculating Brownian diffusion (J_B) for all particles, where

$$J_B = 0.114(\gamma \kappa^2 T^2 / \eta^2 a^2 L)^{1/3} \ln(\phi_w / \phi_b);$$

calculating inertial lift (J_l) for all particles, where $J_l = 0.036 \rho a^3 \gamma^2 / \eta$;

calculating shear induced diffusion (J_s) for all particles, where $J_s = 0.078(a^4/L)^{1/3} \gamma \ln(\phi_w / \phi_b)$, wherein γ is wall shear rate (s^{-1}), κ is Boltzmann constant ($J/mol K$), T is temperature (K), η is bulk fluid viscosity (kg/m.s), a_i is radius of species i (m), L is tube length (m), ϕ_w is particle volume fraction at the membrane wall (-), ϕ_b is the particle volume fraction in the bulk suspension (-), and ρ is particle density (kg/m^3);

determining a J_{max} value for each particle size; and

selecting a J_{max} value from among all J_{max} values that is the lowest, thereby selecting the minimum permeation flux (J).

51. (Currently Amended) The method according to claim 40, wherein said determining packing density at the membrane wall (ϕ_{wj}) for all particles at the predicted permeation flux (a_j for $j \neq i$) comprises:

back-calculating the value of ϕ_{wj} such that ϕ_{wj} gives the predicted permeation flux (J) of selected particle size (a_i), using the equation for back-transport that establishes maximum back transport for each particle size (a_j for $j=i$), wherein the equation is either $J_B = 0.114(\gamma\kappa^2 T^2 / \eta^2 a^2 L)^{1/3} \ln(\phi_w / \phi_b)$ or $J_S = 0.078(a^4 / L)^{1/3} \gamma \ln(\phi_w / \phi_b)$, or $J_I = 0.036 \rho a^3 \gamma^2 / \eta$, where γ is wall shear rate (s^{-1}), κ is Boltzmann constant ($J/mol K$), T is temperature (K), η is bulk fluid viscosity ($kg/m.s$), a_i is radius of species i (m), L is tube length (m), ϕ_w is particle volume fraction at the membrane wall (-), ϕ_b is the particle volume fraction in the bulk suspension (-), and ρ is particle density (kg/m^3).

52. (Original) The method according to claim 51, wherein said determining packing density further comprises:

determining if the predicted permeation flux is established by inertial lift (J_I) for one particle type;

determining if $u_{J_I} \geq 10J$; and

setting $\phi_{wj} = 0$, when one particle type is established by inertial lift (J_I) and $u_{J_I} \geq 10J$.

53. (Original) The method according to claim 51, wherein said determining packing density further comprises:

determining if the predicted permeation flux is established by inertial lift (J_I) for one particle type;

determining if $u_{J_I} < 10J$; and

determining packing density (ϕ_{wj}) by $\phi_{wjI} = \phi_M - \sum \phi_{wj}$ when $u_{J_I} < 10J$ and one particle type is established by inertial lift.

54. (Original) The method according to claim 51, wherein said determining packing density further comprises:

determining if permeation flux is established by inertial lift (J_I) for more than one particle type;

determining if $u_{J_I} < 10J$ for the particles; and

determining packing density by $\phi_{wjl} = \phi_M - \sum \phi_{wj}$ when $u_{jl} < 10J$ and permeation flux is established by inertial lift for more than one particle type.

55. (Original) The method according to claim 51, wherein said determining packing density further comprises:

determining if permeation flux is established by J_1 for more than one particle type ($jl1, jl2, \dots, jl_n$); and

determining packing density at the membrane wall by

$\phi_{wj11} + \phi_{wj12} = \phi_M - \sum \phi_{wj}$, wherein $\phi_{wj11} : \phi_{wj12} = \phi_{bj11} u_{jl1} : \phi_{bj12} u_{jl1}$, where $j \neq jl1$ or $jl2$ and $u_{jl1}, u_{jl2} < 10J$, when permeation flux is established by J_1 for more than one particle type.

56. (Original) The method according to claim 40, wherein filtration is selected from the group consisting of microfiltration and ultrafiltration.

57. (Currently Amended) A method for crossflow membrane filtration of a poly-disperse suspension, said method comprising:

selecting a poly-disperse suspension having a distribution of particle sizes;

determining minimum pore diameter ($2r_{\min}$) based on the packing density of each particle size;

estimating yield of a target species in the filtration permeate for the poly-disperse suspension during crossflow filtration by calculating observed sieving coefficient (S_o) for the target species;

optimizing conditions for filtration based on yield of the target molecule species to design a filtration system for the said poly-disperse suspension; and

filtering the selected poly-disperse suspension using the designed filtration system.

58. (Original) The method according to claim 57, further comprising: refining the yield and pressure independent permeation flux.

59. (Original) The method according to claim 57, wherein said refining the yield comprises:

determining whether the suspension has a low, intermediate, or high operating shear rate leading to different yield regimes, wherein a suspension at a low operating shear rate leads to an $S_o \geq 0.75$ corresponding to a yield ≥ 0.95 , an intermediate operating shear rate leads to $0 < S_o < 0.75$ corresponding to yield from 0 to 95%, or a high operating shear rate leads to an $S_o \cong 0$, wherein $S_o = S_a / ((1 - S_a) \exp(-J/k) + S_a)$, wherein actual sieving coefficient S_a is obtained from $S_a = (S_x \exp(Pe_m)) / (S_x + \exp(Pe_m) - 1)$, wall Peclet number, Pe_m is obtained from $Pe_m = (J \delta_m / D) (S_x / \varepsilon \phi K_d)$, where J is permeation flux (m/s), δ_m is taken as the side of the face centered cube of the particles of radius a ; that forms the controlling cake for transmission, where $\delta_m = a = a_i [4(4/3)\pi / \phi_{\text{interstice}}]^{1/3}$, D is molecular diffusion coefficient (m²/s), intrinsic sieving coefficient S_x is obtained from $S_x = (1 - \lambda)^2 [2 - (1 - \lambda)^2] \exp(-0.7146\lambda^2)$, $\lambda = r_s / r_{\min}$, where r_s is solute radius (m) and r_{\min} is a minimum equivalent cake void radius for all cake types (m), ϕ is equilibrium partition coefficient between membrane pore and suspension (-), ε is cake/membrane porosity (-), K_d is hindrance factor for diffusive transport (-), and k is mass transfer coefficient (m/s).

60. (Original) The method according to claim 59, wherein an intermediate operating shear rate is determined as leading to $0 < S_o < 0.75$, said method further comprising:
calculating stagnant film flux (J) equation for non-retentive membranes wherein $J = k \ln [(\phi_{wi} - \phi_{\text{permeatei}}) / (\phi_{bi} - \phi_{\text{permeatei}})] \cong k \ln [\phi_{wi} / \phi_{bi} (1 - S_o)]$, wherein $(\phi_{wi} \gg \phi_{\text{permeatei}})$; and
correcting S_o by replacing $J = \text{solvent permeation flux (m/s)}$ with the stagnant film flux (J) equation for non-retentive membranes in the equation for observing sieving coefficient, S_o , where $S_o = S_a / ((1 - S_a) \exp(-J/k) + S_a)$.

61. (Original) The method according to claim 57, wherein determining minimum pore diameter ($2r_{\min}$) is carried out using

$$2r_{\min} = a_i \{ \sqrt{2} [4(4/3)\pi / \phi_{\text{interstice}}]^{1/3} - 2 \},$$
 where a is the radius of species i (m) and r_{\min} is a minimum equivalent cake void radius for all cake types (m).

62. (Original) The method according to claim 57, wherein said estimating yield of a target species comprises:

calculating observed sieving coefficient (S_o), where

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$S_o = S_a / ((1 - S_a) \exp(-J/k) + S_a)$, wherein actual sieving coefficient S_a is obtained from $S_a = (S_r \exp(Pe_m)) / (S_r + \exp(Pe_m) - 1)$, wall Peclet number, Pe_m is obtained from $Pe_m = (J \delta_m / D) (S_r / \varepsilon \phi K_d)$, where J is permeation flux (m/s), δ_m is taken as the side of the face centered cube of the particles of radius a ; that forms the controlling cake for transmission, where $\delta_m = a = a_i [(4(4/3)\pi)/\phi_{interstice}]^{1/3}$, D is molecular diffusion coefficient (m²/s), intrinsic sieving coefficient S_r is obtained from $S_r = (1 - \lambda)^2 [2 - (1 - \lambda)^2] \exp(-0.7146\lambda^2)$, $\lambda = r_s/r_{min}$, where r_s is solute radius (m) and r_{min} is a minimum equivalent cake void radius for all cake types (m), ϕ is equilibrium partition coefficient between membrane pore and suspension (-), ε is cake/membrane porosity (-), K_d is hindrance factor for diffusive transport (-), and k is mass transfer coefficient (m/s).

63. (Original) The method according to claim 57, wherein crossflow filtration is carried out in a diafiltration mode, said the yield of the target species after N_d diavolumes is estimated by Yield = 1 - $\exp(-N_d S_{o,average})$, where $S_{o,average}$ is average observed sieving coefficient during diafiltration (-), where $S_o = S_a / ((1 - S_a) \exp(-J/k) + S_a)$, where actual sieving coefficient S_a is obtained from $S_a = (S_r \exp(Pe_m)) / (S_r + \exp(Pe_m) - 1)$, wall Peclet number, Pe_m is obtained from $Pe_m = (J \delta_m / D) (S_r / \varepsilon \phi K_d)$, where J is permeation flux (m/s), δ_m is taken as the side of the face centered cube of the particles of radius a ; that forms the controlling cake for transmission, where $\delta_m = a = a_i [(4(4/3)\pi)/\phi_{interstice}]^{1/3}$, D is molecular diffusion coefficient (m²/s), intrinsic sieving coefficient S_r is obtained from $S_r = (1 - \lambda)^2 [2 - (1 - \lambda)^2] \exp(-0.7146\lambda^2)$, $\lambda = r_s/r_{min}$, where r_s is solute radius (m) and r_{min} is a minimum equivalent cake void radius for all cake types (m), and ϕ is equilibrium partition coefficient between membrane pore and suspension (-), ε is cake/membrane porosity (-), K_d is hindrance factor for diffusive transport (-), and k is mass transfer coefficient (m/s).

64. (Original) The method according to claim 57, wherein filtration is selected from the group consisting of microfiltration and ultrafiltration.

65. (Original) The method according to claim 57, wherein filtration is carried out with a filter selected from the group consisting of a flat sheet filter, hollow-fiber filter, and a helical filter.

66. (Original) The method according to claim 57, wherein the suspension is selected from the group consisting of streams from biomedical and bio-processing industries, waste water, surface water, environmental pollutants, industrial waste streams, and industrial feed streams.

67. (Original) The method according to claim 66, wherein the suspension is a stream from biomedical and bio-processing industries selected from the group consisting of proteins, cells, nucleic acids, colloids, milk, and suspended particles.

68.-72. (Cancelled)

73. (Original) The method according to claim 40, wherein filtration is carried out with a filter selected from the group consisting of a flat sheet filter, hollow-fiber filter, and a helical filter.

74. (Previously Presented) The method according to claim 40, wherein the suspension is selected from the group consisting of waste water, surface water, environmental pollutants, industrial waste streams, and industrial feed streams.

75.-79. (Cancelled)

80. (Previously Presented) The method according to claim 30, wherein filtration is carried out with a filter selected from the group consisting of a flat sheet filter, hollow-fiber filter, and a helical filter.

81. (Previously Presented) The method according to claim 30, wherein the suspension is selected from the group consisting of streams from biomedical and bio-processing industries, waste water, surface water, environmental pollutants, industrial waste streams, and industrial feed streams.

82. (Previously Presented) The method according to claim 81, wherein the suspension is a stream from biomedical and bio-processing industries selected from the group consisting of proteins, cells, nucleic acids, colloids, milk, and suspended particles.

83. (Previously Presented) The method according to claim 74, wherein the suspension is a stream from biomedical and bio-processing industries selected from the group consisting of proteins, cells, nucleic acids, colloids, milk, and suspended particles.

Authorization for this examiner's amendment was given in a telephone interview with Michael Goldman on July 14, 2009.

The following is an examiner's statement of reasons for allowance: The claims are distinguished over all of the prior art, for reasons of record, summarized in the Remarks accompanying Applicant's 5/1/2009 Amendment. The changes made by Examiner's Amendment were made to mitigate a plurality of 112, paragraph 2 problems concerning inconsistent terminology and antecedent basis. Support can be found in the claims as originally found and at Paragraphs 8 and 9 of the Instant Specification.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

JWD
7/16/2009
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/P. R./
Supervisory Patent Examiner, Art Unit 1795